

# KIDNEY DISEASE IN NATIVE AMERICANS

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Over the past few decades, the disease burden among American Indians and Alaska Natives (AI/AN) has shifted from acute infectious diseases to chronic illnesses, particularly type 2 diabetes and its complications. AI/ANs experience high rates of end-stage renal disease (ESRD), mainly driven by the increase in diabetes. The prevalence of ESRD is 3.5 times greater than that in white Americans.

The burden of ESRD has become a community-wide problem among many tribes, and significant efforts have gone into establishing dialysis services on reservations. Reservation-based dialysis services have improved the access of patients to renal replacement therapy, but enormous barriers to improving care remain. These include: the rural and frequently isolated locations that make traveling to facilities difficult owing to distance and road conditions; high rates of poverty; difficulty in recruiting and retaining staff in outlying areas; language and cultural differences; and the high numbers of patients with diabetes and extra-renal diabetic complications.

Disparities exist in access to kidney transplantation, with AI/ANs waiting longer for organs than their white counterparts. However, once transplanted, they have comparable survival rates to white Americans.

An aggressive approach to intervention, which includes prevention and optimal therapy, is required to slow the growth of ESRD amongst AI/ANs.

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There are approximately 2.5 million people that identify themselves as American Indians or Alaska Natives (AI/AN). The AI/AN population includes members of more than 550 federally recognized tribes, representing diverse cultural traditions and lifestyles. Approximately 38% of the AI/AN pop-

ulations live on rural reservations, mostly in the western United States, and 22% live near reservations. Tribes function as sovereign nations and relate to the federal government on a nation-to-nation basis. The American-Indian population is relatively young, with a median age of 27.8 years (compared with 35.8 years for the all races in the United States), and relatively poor with 32% living below the poverty rate (compared with 13.1% of the US population). Unemployment is twice as high and income is two-thirds of that of the rest of the country.<sup>1</sup>

Over the past few decades the disease burden among AI/AN has shifted from acute infectious diseases to chronic illnesses, particularly type 2 diabetes and its complications. Diabetes, a condi-

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tion virtually unknown prior to World War II, has reached epidemic proportions among the native people of North America. Its prevalence is 2.8 times the rate among US non-Hispanic whites,<sup>2</sup> and 9% of all AI/AN aged 20 years and older are diabetic. In some tribes (e.g. Pima, Zuni), 30% to 50% of the population are diabetic. Among Navajo people aged over 45 years, 40% are diabetic.<sup>3</sup> Diabetes rates are rising across all age groups, with the most alarming increase in adolescents and young adults, where its prevalence increased by 32% in 15- to 19-year-olds between 1991 and 1997.<sup>4</sup> Diabetes mortality among AI/AN (39.4 per 100,000 population) is three times higher than in the US population (13.3 per 100,000 population).

Most AI/AN living on reservations and some living in urban centers receive healthcare through the Indian Health Service (IHS), an agency of the US Public Health Service. The IHS is the principal federal healthcare provider and health advocate for Indian people and provides health services to approximately 1.5 million people, with a budget of approximately \$2.5 billion.

## **BURDEN OF KIDNEY DISEASE**

### **End-Stage Renal Disease**

AI/AN experience high rates of end-stage renal disease (ESRD), driven by the increase in diabetes. From 1988 to 1997 the number of AI/AN with ESRD tripled, and by the end of 1999, its prevalence was 3.5 times greater than that of white Americans.<sup>5</sup> Over two-thirds (68%) of AI/AN who initiated ESRD treatment in 1999 developed kidney failure due to diabetes, virtually all type 2, while only 25% of whites and 42% of blacks with ESRD were diabetic. The incidence rate for ESRD due to type 2 diabetes among AI/AN during 1996 to 1999 (349 per million) was three times that of the rate in whites (99 per million). Also, it was higher than any other disease-specific rate for any US race, with the incidence being substantially higher in AI/AN women (394 per million) than in men (304 per million). Consistent with the early onset of type 2 diabetes among native people, the mean age at onset of ESRD is 57 years, six years younger than for whites (63 years).

Significant regional variations are masked among the many tribes that make up the AI community. The burden of kidney failure is higher among AI/AN of the Southwest. While the overall US rate of treated ESRD was 3.2 times greater among AI/AN than among whites, in the Southwest it was 6.5 times greater. Ninety-two percent of the Southwest ESRD patients were full-blood quantum AI/AN (all four grandparents are AI/AN). In Zuni Pueblo, a western New Mexico community, the prevalence of ESRD is 17,400 per million population,<sup>6</sup> which is 4.5-, 5.7-, and 21.3-fold higher than that of African Americans, AI, and European Americans, respectively.

## **Chronic Kidney Disease**

Several studies have demonstrated increased rates of early kidney disease among AI/AN, both in diabetics and non-diabetics. The Strong Heart Study, a longitudinal study to measure risk factors for cardiovascular disease among American Indians from three geographic sites (Arizona, North and South Dakota, and Oklahoma), has demonstrated high rates of abnormal albumin excretion (20.1% to 48.3%) in all tribes studied.<sup>7</sup> Although the prevalence of diabetes was 53% in the study population, 10% to 20% of patients without diabetes had albuminuria. Among both diabetics and non-diabetics, abnormal albumin excretion was associated with increased blood quantum (degree of Indian heritage), suggesting a genetic basis for susceptibility to kidney injury. The Zuni Kidney Project, a population-based, cross-sectional survey of the Pueblo of Zuni, has also demonstrated albuminuria in 20% of the population, only half of whom were diabetic.<sup>8</sup>

Determining the burden of non-diabetic kidney disease is problematic in a population where 30% to 50% of the adult population may be diabetic, because many cases of non-diabetic kidney disease may also have diabetes as a comorbid condition. In these cases, nephrologic evaluation might be delayed until late in the course of the kidney injury, when biopsy is no longer a consideration, and physicians may incorrectly assume that the primary cause of kidney failure is diabetes.

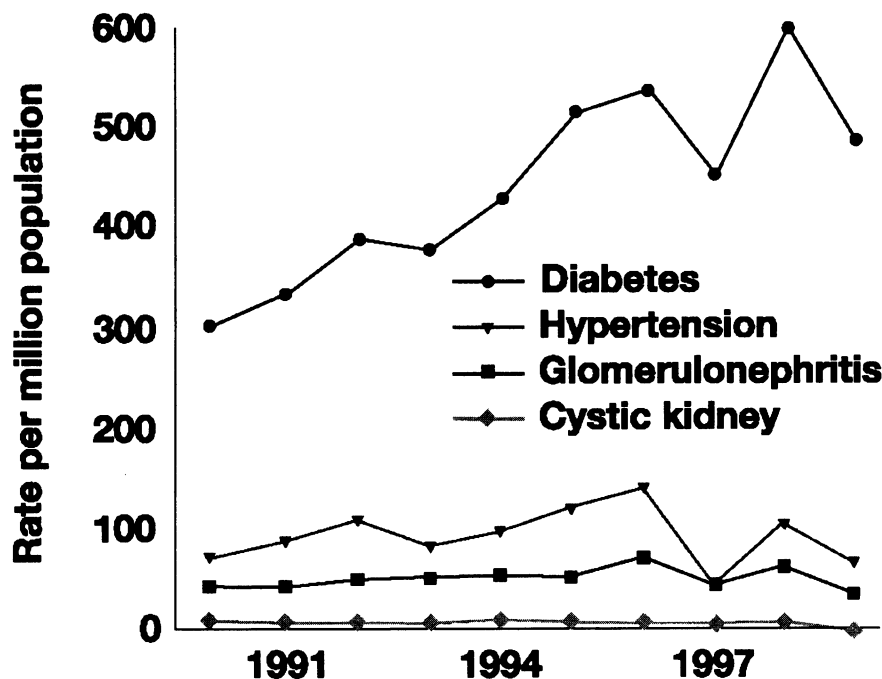
Studies of the Zuni Pueblo reported high rates of mesangiopathic glomerulonephritis (MesGN), predominantly immunoglobulin (Ig) A.<sup>9</sup> A biopsy series from Zuni people with non-diabetic kidney disease included 77% with MesGN. Immunoglobulins and complement and well-defined electron-dense deposits were present in the mesangium in half of these cases. IgM, IgA, IgG, and complement component C3 were variably represented. A review of all AI renal biopsies processed at the University of New Mexico Health Sciences Center from 1971 to 1989 included 166 specimens, 64 of these were from Zuni people. Immunoglobulin-positive MesGN, mesangial expansion and/or mesangial cell proliferation, together with mesangial immune deposits were diagnosed in 78% of the Zuni specimens; nearly 40% showed cellular crescents.<sup>10</sup>

The burden of diabetic nephropathy has been

monitored for several years by the IHS Diabetes Program.<sup>11</sup> Abnormal protein excretion was present in 33% of the patients, of whom 10% had microalbuminuria and 23% had overt proteinuria. Hypertension was present in 77% of those with overt proteinuria and 69% of those with microalbuminuria.

### TREATMENT OF ESRD

For many tribes, the burden of ESRD has become a community-wide problem, and significant efforts have gone into establishing dialysis services on reservations. By the end of 2000 there were more than 30 dialysis units on or near reservations serving predominantly AI/AN patients.<sup>12</sup> Although reservation-based dialysis units have improved the access of patients to renal replacement therapy, enormous barriers to improving care remain. These include the rural and frequently iso-



**Figure 1.** Incident Rates of Kidney Disease in Native Americans by Primary Diagnosis in Dialysis Patients, Adjusted for Age and Gender. Following the general trends in dialysis patients as a whole, rates of diabetes have increased across all races, and the disease continues to be the primary cause of ESRD.<sup>5</sup>

lated locations that make traveling to facilities difficult due to distance and road conditions, high rates of poverty, difficulty in recruiting and retaining staff in outlying areas, language and cultural differences, and the high numbers of patients with diabetes and extra-renal diabetic complications. A recent survey of the 524 AI/AN dialysis patients aged 20 to 60 years living in Arizona and New Mexico revealed that 80% lived on a reservation, 31% had only an elementary education, 73% did not speak English at home, and 56% traveled more than an hour each way for dialysis treatment.<sup>13</sup>

## ACCESS TO TRANSPLANTATION

At the end of 1999, only 22% of the AI/AN ESRD population had functioning transplants, compared with 36% of white patients. The rate of kidney transplants was 0.7 transplants per 100 patient-years on dialysis, while the rate for white patients was 1.8 transplants per 100 patient-years on dialysis. According to the Health Care Financing Administration AI/AN patients are less likely than whites to be placed on the transplant waiting list, and those listed wait longer for a transplant. Similar results were found in studies by ESRD Network #15 in Arizona and New Mexico.<sup>13</sup> Delays in completing transplant evaluations play a significant role in the low access to transplantation for at least some racial and economic minorities. ESRD Network #15 and the IHS examined socio-demographic factors, ESRD treatment, comorbidities, and transplant candidacy status to determine the factors that contribute to candidacy and whether the AI/AN ESRD population experiences barriers not encountered by the white population. Using six different criteria, studies showed that the rates of candidacy for AI/AN and white patients were about the same by every definition except the most stringent: the time awaiting transplant.

The major barriers for AI/AN patients lie in the process of fulfilling requirements and in the availability of matching kidneys. Data obtained from the United Network for Organ Sharing (UNOS) indicate that the Kaplan-Meier median waiting time to transplant for patients from Arizona and

New Mexico listed during 1997 through 1999 was 1306 days for AI/AN and 929 days for whites. After six months on the waiting list, 6.2% of the AI/AN patients and 11.1% of white patients had received a transplant. Although a higher proportion of AI transplant recipients in the ESRD Network #15 have a living, related donor allograft than white recipients, cadaver donation from AI/AN remains a rare event. Significant cultural barriers will have to be overcome to increase the donation rate. Thus, AI/AN are referred for transplant at similar rates to white patients, but experience a greater delay before transplantation.

Unlike African Americans, another minority group with low transplant rates, graft survival in AI/AN compares favorably with that of whites. UNOS reports that both patient and graft survival were slightly, though not statistically, better among AI/AN than among whites in Arizona and New Mexico during the 1997 to 1999 period.

## SURVIVAL WITH ESRD

Despite socio-economic barriers and high rates of comorbid illness, survival among AI/AN patients is better than among whites. The 1999 US Renal Data System reports a mortality rate for prevalent dialysis patients of 196.7 per 1000 patient-years for whites and 162.4 per 1000 patient-years for AI/AN. Although the mean albumin of AI/AN persons starting dialysis from 1995 to 2000 (3.0 g/dL) was lower than for whites (3.2 g/dL), body mass index, which may also predict survival, was higher (26.8 kg/m<sup>2</sup>) than for whites (25.8 kg/m<sup>2</sup>).

## PREVENTION/EARLY INTERVENTION

Diabetes is the predominant cause of the excess burden of ESRD among AI/AN, and the IHS has committed significant resources to address diabetes and its complications. Although the HIS only receives 40% of per capita funding compared with that provided for the US civilian population through private insurance and other programs (\$1578 versus \$3920/year), it has been aggressive in implementing and monitoring optimal care for diabetic patients who are at risk of

chronic kidney disease. This has enabled IHS providers to be more successful in achieving benchmarks of clinical care for diabetic nephropathy than other large providers.<sup>11</sup>

The effectiveness of the IHS in achieving this level of care suggests the potential benefit of approaching kidney disease using a public health model. Such a model includes a multidisciplinary clinical approach integrated with community-based interventions.

## FUTURE RESEARCH

The epidemic of type 2 diabetes, which has affected AI/AN communities for 50 years, is now being duplicated in other 'emerging' groups worldwide and in the populations of highly industrialized countries. This suggests that AI/AN are not an aberrant group but merely "ahead of their time." The natural history of diabetic nephropathy has been well studied in the Pima Indians and has been utilized in understanding other populations. Native health leaders frequently express the desire that further efforts will be made to research effective preventive interventions that will have a similar wide application.

Some research questions to be addressed in the near future include:

- Is there increased susceptibility to non-diabetic kidney injury among AI/AN?
- Why is the incidence of ESRD increasing among AI women with diabetes?
- Why is survival on dialysis better for AI/AN than for non-AI/AN populations despite low initial albumin?
- What is the most cost-effective way to deliver care to CKD patients in high-risk populations?

There is a sense of urgency among tribal leaders to address the epidemic of kidney disease in AI/AN, and research that may decrease its burden is likely to be welcomed.

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